REMARKS

Summary of Telephonic Interview with Examiner

Applicants and their attorney thank Examiners Gupta and Niebauer for the courtesy of the telephonic interview conducted on September 18, 2008 during which the outstanding rejections under 35 U.S.C. § 112, first and second paragraphs and the priority matter were discussed.

Amendments to the Claims

Claims 49-54, 57-66 and 69-73 were pending in the instant application as of the issuance of the Office Action dated March 18, 2008. Claims 49-50, 69 and 71-73 stand rejected. Claims 51-54, 57-66 and 70 have been withdrawn as allegedly "being drawn to a nonelected species, there being no allowable generic or linking claim." According to the foregoing amendments, claims 49-51 have been amended. Accordingly, after the amendments presented herein have been entered, claims 49-54, 57-66 and 69-73 will remain pending in this application.

Support for the amendments to the claims may be found throughout the specification and in the claims as originally filed. Specifically, support for the amendments to claims 49 and 50 can be found throughout the specification at, for example, page 32, line 16 to page 33, line 25 and page 35, line 11 to page 39.

No new matter has been added by the amendments to the claims. The amendments to the claims should not be construed as an acquiescence to the validity of the outstanding rejections and were done solely in the interest of expediting prosecution and allowance of the claims. Applicants reserve the right to pursue the claims as previously pending and as originally filed in one or more further applications.

Priority

The Office Action sets forth that claims 49-51 as previously presented do not find support in the specification as originally filed on the grounds that

> the claims as amended (49-51 and dependent claims) recite a particular subgenus that is not supported by the original application... Page 33 lines 22-25 recite a condition for X_9, but do not recite the subgenus of the current claims. For example, page 33 lines 10 and 13 support a peptide in which R is replaced and X_6 is replaced. However, claims 49-50

> support a subgenus in which R can be unchanged (i.e. does not agree with original disclosure of R is replaced). Claims 49-51 support a subgenus in which X_6 can be unchanged (i.e. does not agree with original disclosure of X_6 is replaced). Although applicants claim support from claims 67-68 as originally filed, there were no claims 67-68 as originally filed. Hence, claims 49-55, 57-66 [and] 69-70 do not receive the priority date of the originally filed application.

Applicants respectfully disagree. Applicants submit that the present application as originally filed, in addition to the originally filed specification of priority U.S. Application No. 10/441952, filed May 19, 2003, the teachings of which are incorporated by reference into the present application, each provide sufficient support for the claimed peptides. Notwithstanding the foregoing, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended independent claims 49 and 50, support for which can also be found in the teachings of the present application and, further, in priority U.S. Application No. 10/441952.

Applicants respectfully submit that the Examiner's characterization of the specification and specifically, the embodiments of the invention as set forth on page 33, lines 8-25 and on page 34, line 19 to page 35, line 5 of the present specification (and on page 36, line 6 to page 39, line 13 of priority U.S. Application No. 10/441952) is incorrect. Applicants submit that while the Examiner has interpreted, for example, the teachings of page 33, lines 8-25, as requiring that the peptides of the invention have each of the features set forth in items (a) – (e), such interpretation is contrary to the teachings of the specification, as would be understood by one skilled in the art. Indeed, Applicants submit that the teachings of the specification ***do not, in fact, require that the disclosed embodiment comply with each of the features set forth in items (a) – (e)***. Instead, the specification provides such features as alternatives, one or more of which may be applicable.

Applicants submit that the context of the teachings of the specification confirms such interpretation of the present specification. Applicants once again direct the Examiner's attention to the specific pentapeptides listed in the application, see, for example, page 35, line 11 through page 39. ***Applicants submit that the only interpretation of the specification that would allow for the recited species of pentapeptide variants of SEQ ID NO:293 to be consistent with and to fall within the scope of the recited genus of variants as set forth on page 33, lines 8-25 is one in which the recited features are deemed to be alternatives and not required in combination.***

For example, all but one of the recited pentapeptides on pages 35-39, specifically, SEQ ID NOs:294-375 and 377, which Applicants note are referred to as "peptides of the formula V (SEQ ID NO:293), ***or variants thereof***," require an arginine at position one of the pentapeptide. The remaining pentapeptide, *i.e.*, SEQ ID NO:376, has a leucine at the X_7 residue. ***If the Examiner's interpretation of the specification is adopted, one in which each of the recited features on page 33, lines 8-25, is deemed to be required, then, for example, variants of SEQ ID NO:293 cannot have arginine at position one and cannot have leucine at position X_7 as these residues must be replaced. Accordingly, the recited pentapeptide variant species in the specification would conflict with the general description of variants as set forth in the specification. However, adopting Applicants' interpretation of the specification, one in which each of the recited features on page 33, lines 8-25, is deemed to be an alternative, would allow for the recited pentapeptide variant species to be consistent with and fall within the scope of the described genus of variants.*** Accordingly, the listing and nature of numerous pentapeptide variant species in the present application demands a construction of the features described at page 33, lines 8-25 as alternatives to each other and not required in combination.

Applicants further note that, as acknowledged by the Examiner, the M.P.E.P. § 2163(II)(A)(3)(b) sets forth the following standard for determining whether support exists in the specification of an application or a priority document:

> [t]o comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c), each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure. When an explicit limitation in a claim 'is not present in the written description whose benefit is sought it must be shown that a person of ordinary skill would have understood, at the time the patent application was filed, that the description requires that limitation.' *Hyatt v. Boone*, 146 F.3d 1348, 1353... (Fed. Cir. 1998).

Indeed, the claimed genus of molecules may be supported either explicitly, implicitly or inherently by the teachings of the specification. The appropriate perspective in ultimately determining support with respect to priority and written description is that of a skilled artisan upon reading the teachings of the specification. Applying such standard to the present case, Applicants submit that the claimed genus of peptides is sufficiently supported both by the explicit and implicit teachings of the present specification and, further, the teachings of priority U.S. Application No. 10/441952, each taken in proper context, as would be understood by a skilled artisan and as elucidated above. Indeed, Applicants submit that one skilled in the art

would appreciate that the teachings of the specification make clear that the recited features are exemplary and not required together in combination.

In support of his interpretation of the excerpt at page 33, lines 8-25 of the specification, the Examiner states that "each of (a)-(e) (page 33, lines 10-25) recite that each of R/X6/X7/X8/X9 **is** replaced (the claims do not recite a or b or c or d or e)." Applicants respectfully disagree with the Examiner's characterization of this excerpt and the conclusions drawn therefrom. Applicants acknowledge that in setting forth each option for variation with respect to R, X6, X7, X8 and X9, the specification recites that "R is replaced...," "X6 is replaced...," etc. However, the specification does not state that "each of" R, X6, X7, X8 and X9 are replaced, as the Examiner suggests. In addition, such recitation in the specification is not tantamount to requiring each recited residue being replaced in combination, as the Examiner suggests. In fact, Applicants submit that such recitation is not inconsistent, and, moreover, is consistent with Applicants' construction of the excerpt as reciting alternatives. Furthermore, the context of the specification conclusively establishes that the excerpt should be read as reciting alternatives, as detailed above.

In view of the foregoing standard, and, further, in light of the foregoing arguments and those previously on record, Applicants submit that the specification of the present application and, further, the specification of the priority document (U.S. Application No. 10/441952, filed May 19, 2003) provide ample support for the pending claims. Accordingly, Applicants submit that the claims as amended are entitled to priority at least as early as the filing of U.S. Application No. 10/441952 on May 19, 2003.

Rejection of Claims 49, 50 and 69 Under 35 U.S.C. § 112, Second Paragraph

Claims 49, 50 and 69 have been rejected under 35 U.S.C. § 112(b), second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Office Action sets forth that

> [t]he claims refer to a peptide of SEQ ID NO:293 which as defined on page 32 of the specification (line 22), states that X_9 is Phe. Further, in the sequence listing provided it is stated that the position corresponding to X9 is Phe. As such, X9 must be Phe not Cha, Hof, pFPhe, etc. as in claims 49-50,69.

Applicants note that solely in the interest of expediting prosecution and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended independent claims 49 and 50 to be directed to a "peptide consisting of ***a variant of*** formula V, $RX_6X_7X_8X_9$ (SEQ ID No. 293)" wherein each of the particular residues are specifically defined, thereby rendering the foregoing rejection moot. Applicants submit that support for the foregoing amendments can be found throughout the specification as originally filed, for example, at page 32, line 16 to page 33, line 25. Indeed, as set forth in the specification and in the sequence listing, SEQ ID NO:293 refers to a peptide of formula V ($RX_6X_7X_8X_9$), wherein X_6 is arginine, serine or lysine; X_7 is leucine, isoleucine or valine; X_8 is asparagine, alanine, glycine or isoleucine; and X_9 is phenylalanine. However, as taught on page 33, lines 8-25, the invention is further directed to a variant of SEQ ID NO:293 in which any of the residues are modified as set forth therein. In a particular embodiment, X_9 is modified to be "a natural or unnatural amino acid selected from the group consisting of leucine, cyclohexylalanine (Cha), homophenylalanine (Hof), tyrosine, parafluorophenylalanine (pFPhe), metafluorophenylalanine (mFPhe), tryptophan, 1-naphthylalanine (1Nal), 2-naphthylalanine (2Nal), metachlorophenylalanine (mClPhe), biphenylalanine (Bip) and 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic)."

Such interpretation of the specification, as reflected in the pending claims, is buttressed by the presence of particular pentapeptide variants of SEQ ID NO:293 set forth on page 35, lines 11 to page 39 of the specification. Numerous species of pentapeptide variants of SEQ ID NO:293 are disclosed, for example, where X_9, alone, is modified in accordance with the limitations of claims 49-50. For example, each of SEQ ID NOs:295, 296, 298, 299, 301, 302, 304, 305, 307, 308, 310, 311, 313, 314, 316, 317, 319, 320, 322, 323, 325, 326, 328, 329, 331, 332, 334, etc. are species of the claimed genus of pentapeptide variant of SEQ ID NO:293, where X_9, alone, is modified relative to SEQ ID NO:293.

Applicants direct the Examiner's attention to the discussion under the "Priority" section set forth above, further supporting Applicants' contention that the present claims are supported by the specification of the present application and of priority U.S. Application No. 10/441952, filed May 19, 2003.

Based at least on the foregoing, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 49, 50 and 69 Under 35 U.S.C. § 112, First Paragraph

Claims 49, 50 and 69 have been rejected under 35 U.S.C. § 112(b) first paragraph as "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Office Action sets forth that

> [t]he specification is void of any literal support for the subgenus of peptides claimed. Page 33 lines 22-25 recite a condition for X_9, but do not recite the subgenus of the current claims It is noted that each of (a)-(e) (page 33 lines 10-25) recite that each of R/X6/X7/X8/X9 **is** replaced (the claims do not recite a or b or c or d or e) with amino acids other than those as recited in the instant claims. As such the subgenus of peptides are not literally defined...
>
> For example, page 33 lines 10 and 13 support a peptide in which R is replaced and X_6 is replaced. However, claims 49-50 support a subgenus in which R can be unchanged (i.e. does not agree with original disclosure of R is replaced). Claims 49-51 support a subgenus in which X_6 can be unchanged (i.e. does not agree with original disclosure of X_6 is replaced).
>
> Since the specification teaches that each of R/X6/X7/X8/X9 **is** replaced (the claims do not recite a or b or c or d or e) one would not interpret (as applicant contends) such disclosure as, for example, R is not replaced X6 is not replaced but X9 is replaced...
>
> In the instant case, the broad disclosure (specification page 32 line 25-27) is such that nearly any peptide imaginable would fall within the scope and as such one would not be lead to the particular subgenus that is currently claimed. It is noted that page 32 lines 25-27 recites that at least one of a deletion, addition, or substitution, of one or more amino acid residues is possible... As such, one would not be lead to the subgenus as currently claimed. Further, although examples are provided in the specification the examples do not include Cha, Hof, tyrosine, tryptophan, 1nal, 2nal, Bip, or Tic at the X9 position as currently claimed.

Applicants respectfully disagree. In support, Applicants direct the Examiner's attention to the foregoing discussion under the section entitled "Priority" and, further under the section entitled "Rejection of Claims 49, 50 and 69 Under 35 U.S.C. § 112, Second Paragraph" in which Applicants detail how the present specification and priority U.S. Application No. 10/441952, the teachings of which are incorporated by reference to the present specification, provide support for the pending claims. Indeed, in view of the standard set forth in M.P.E.P. § 2163(II)(A)(3)(b), Applicants submit that the teachings of the specification, and, in particular, the teachings of variants at page 33, lines 8-25 and the teachings of particular pentapeptide variants of SEQ ID NO:293 at page 35, line 12 to page 39, provide sufficient support for the claims as pending.

In view of the foregoing discussion and the amendments set forth herein, Applicants respectfully request reconsideration and withdrawal of the pending claims as lacking written description.

Rejection of Claims 49, 50 and 69 Under 35 U.S.C. § 102(b)

Claims 49, 50 and 69 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Publication No. 2005/0260730 to Fischer *et al.* (hereinafter referred to as "Fischer") on the ground that Fischer "teach the peptide H-Arg-Arg-Leu-Asn-pFPhe-NH2 (section 0015 SEQ ID NO:4), the acetylation of peptides (section 0104) and the acylation of peptides (section 0038) thereby meeting the limitations of claims 49-50,69 of the instant invention."

Applicants respectfully traverse the foregoing rejection on the ground that Fischer fails to anticipate the claimed invention. Notwithstanding the foregoing, Applicants submit that Fischer fails to qualify as prior art under 35 U.S.C. § 102(b). Indeed, as set forth above, Applicants submit that the claimed invention is entitled to the priority date of May 19, 2003 and therefore predates the Fischer reference. Accordingly, because Fischer fails to qualify as prior art under 35 U.S.C. § 102, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 49, 50, 69 and 71-73 Under 35 U.S.C. § 103(a)

Claims 49, 50, 69 and 71-73 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Zheleva *et al.* (International Publication No. WO01/40142) (hereinafter "Zheleva") and Mutoh *et al.* (*Cancer Research* (1999) 59:3480-3488) (hereinafter "Mutoh"). Specifically, the Examiner is of the opinion that

> Zheleva teach p21 derived inhibition peptides (abstract). Zheleva specifically teach the peptide H-Ala-Ala-Lys-Arg-Arg-Leu-Asn-pFPhe-NH2 which corresponds to residues 152-159... Zheleva teach that the pFPhe derivative is desirable... as it results in more complementary interactions. Zheleva teach that residues may be deleted from the N-terminal end... for example in one embodiment residues 155-159 are the peptide of interest. Zheleva teach acylation reactions in preparing the peptide...
>
> Zheleva does not expressly teach the elected peptide H-Arg-Arg-Leu-Asn-pFPhe-NH2.
>
> Mutoh et al. teach p21 derived inhibitory peptides (abstract). Mutoh specifically teach that residues 155-159 are important for retention of the inhibitory activity...

> Since Zheleva specifically teach the peptide H-Ala-Ala-Lys-Arg-Arg-Leu-Asn-pFPhe-NH2 which corresponds to residues 152-159 of p21 and further teach that residues may be deleted from the N-terminal end... one would be motivated to delete residues from the N-terminal end. Since Mutoh specifically teach that residues 155-159 of p21 are important for retention of the inhibitory activity... one would be motivated to delete Ala-Ala-Lys from the peptide taught by Zheleva to arrive at H-Arg-Arg-Leu-Asn-pFPhe-NH2 which is the elected species and meets the limitations of claims 49-50, 71-73 of the instant invention. Since Zheleva teach acylation reactions in preparing the peptide... the limitations of claim 69 are met.

Applicants respectfully traverse the foregoing rejection on the ground that the teachings of Zheleva, alone or in combination with Mutoh, fails to anticipate the claimed invention. Applicants submit that the Examiner's rejection is based on impermissible hindsight, contrary to the requirements of MPEP § 2142, and further that the combination of the cited references teach away from the claimed invention.

Initially, Applicants submit that the Examiner's rejection is predicated upon one skilled in the art performing a series of steps based on general statements to eventually arrive at the claimed invention. Indeed, Applicants submit that in order to arrive at the claimed genus of pentapeptides and, in particular, the particular species under examination, one skilled in the art would be compelled to choose one particular species of octapeptide from a list of nearly two hundred disclosed in Zheleva (see, for example, page 12, line 11 to page 15, line 4 and pages 74 and 75) and delete exactly three residues from the N-terminal end based on disclosure setting forth that any of one, two, three, four, five, six or seven amino acids may be deleted (see page 82 and on page 6, lines 6-8). Applicants submit that such modifications and such suggestion are based on impermissible hindsight.

Applicants further submit that the teachings of Mutoh teach away from the claimed invention and the requisite modifications to Zheleva to arrive at the claimed inventions. Applicants direct the Examiner's attention to page 3485 of Mutoh which states:

> Indeed, we found peptides with substitutions that disrupted a potential 3_{10}-helix motif (^{147}SMTDFY^{151} changed to SGSGSG) and a potential β-strand motif (^{153}SKRRLIF^{159} changed to SKAAAIF), and exhibited significantly reduced Cdk-inhibitory activity compared with the native segment W10 peptide... Less predictably, triple alanine mutation at amino acid positions 142-144 in W10 (mutant peptide AM1) also affected inhibitory potency, possibly destroying ionic interactions with the cyclin/Cdk complex. Our results extend beyond the observations reported in the work of Ball et al.... who, using single alanine substitutions, found that the integrity of the ^{155}RRLIF^{159} sequence was important for retention of cyclin D1/Cdk4 inhibitory activity. Our data show for the

first time that disruption of a potential 3_{10} helix in the W10 peptide with amino acid substitutions can markedly affect Cdk-inhibitory activity against both cyclin E/Cdk2 and cyclin D1/Cdk4.

As set forth therein, Mutoh clearly teaches against modification to p21 fragments and, in particular, to the ^{155}RRLIF^{159} fragment. Indeed, Mutoh teaches that modifications have been shown to disrupt the conformational structure of p21 fragments and result in significantly reduced inhibitory activity. Mutoh specifically describes the reduction of inhibitory activity resulting from modification in the ^{155}RRLIF^{159} fragment and reports on the importance of the "integrity" of the ^{155}RRLIF^{159} fragment. As such, Mutoh teaches away from any such modifications to p21 fragments as would be necessary to arrive at the claimed invention, contrary to the requirements of MPEP 2143.01.

Based at least on the foregoing, Applicants submit that the teachings of Zheleva, alone or in combination with Mutoh, fail to render the claimed invention obvious. Accordingly, Applicants respectfully request reconsideration and withdrawal of the outstanding rejection under 35 U.S.C. § 103(a).

Provisional Rejection Under 35 U.S.C. § 101

Claims 71-73 have been provisionally rejected under 35 U.S.C. § 101 "as claiming the same invention as that of claims 20, 21, [and] 22 of copending Application No. 11/407,880."

Applicants respectfully disagree. However, while in no way acquiescing to the outstanding rejection, Applicants note that prosecution of the present application and copending Application No. 11/407,880 may render such rejection moot. Accordingly, Applicants will address such rejection as appropriate upon allowance of the claims in U.S. Application No. 11/407,880 or once the pending claims in the present application are formally indicated as otherwise allowable.

Provisional Rejection Under Judicially Created Doctrine of Obviousness-type Double Patenting

Claims 49, 50 and 69 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 16, 17, 18 and 20-23 of copending Application No. 11/407,880. For example, the 2nd peptide of claim 20 of

11/407,880 reads on claims 49-50 of the instant invention. Claim 23 of 11/407,880 reads on claim 69 of the instant invention."

While in no way acquiescing to the Examiner's rejections under the judicially created doctrine of obviousness-type double patenting, Applicants note that prosecution of the present application and copending Application No. 11/407,880 may render such rejection moot. Accordingly, once the pending claims in the present application are formally indicated as otherwise allowable, and should such submission(s) be necessary, Applicants will submit a terminal disclaimer in compliance with C.F.R. §§ 1.321(b) and (c), as appropriate, which will obviate this rejection.

SUMMARY

Applicants respectfully submit that the above-identified application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the present filing to Deposit Account No. 12-0080 under Order No. CCI-014CP2RCE, from which the undersigned is authorized to withdraw.

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